A Chronic Ontology Model as Clinical Decision Support System for Longitudinal Monitoring of Patients with Bipolar I Disorder

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Abstract

Clinical decision support (CDS) systems are computer systems that deal with scientific knowledge and patient data in order to offer clinical guidance. The utility of CDS systems in mental health can be viewed in terms of enhancing both the diagnosis and treatment processes. Addressing these issues, we exploit Semantic Web Technologies to develop AI-CARE, as a Clinical Decision Support System based on evidence-based clinical guidelines and the patient’s medical information. The AI-CARE approach allows individualized diagnosis and treatment decisions as output of the examined case by providing recommendations about the best therapeutic treatment, notifications and alerts. We present a chronic ontology model based on the longitudinal course of Bipolar I Disorder (BDI) that incorporates acute episodes and treatment algorithms as well as patient-centered factors, with the aim to elaborate on this information and offer regimen choices to clinicians for better mental health care.

Keywords: bipolar disorder, longitudinal monitoring, clinical decision support system, Semantic Web Technologies, AI-CARE.

Introduction

1.1. Background

Bipolar Disorder (BD) is a severe psychiatric illness that exhibits a time-dependent recurrence. The dramatic mood swings between mania and depression that accompany BD cause impacts in every aspect of a patient's life. The high rates of suicide, the accompanying psychiatric and medical comorbidities, as well as the effectiveness of pharmacotherapy and therapeutic compliance in patients with BD, increase the complexity of this chronic illness [1].

To address these issues, advanced health information technologies are needed, including computer-based clinical decision support (CDS) systems. Such systems are designed to improve clinical decision-making by providing clinicians, staff, patients, and other individuals with knowledge and subject-specific information, intelligently filtered and presented at appropriate times, as to enhance health care [2]. To date, in the area of mental health, a computerized decision support system for major depressive disorder treatment, CompTMAP (according to the Texas Medication Algorithm Project) has been developed [3]. CompTMAP based on evidence-based guidelines and algorithms was tested and used to support diagnosis, treatment, follow-up, as well as preventive care.

In the same line of thought, we propose AI-CARE, a computer-based CDS system with application in bipolar I disorder (BDI) that relies primarily on the evidence-based clinical guidelines and individual patient data, while providing an interactive tool that can be used for effective decision making by psychiatrists and other primary healthcare professionals.

1.2. Semantic Web Technologies

We exploit Semantic Web Technologies in order to extract knowledge included in this information and implement the decision mechanism. Semantic Web technologies form a family of very specific technology standards from the World Wide Web Consortium (W3C) that are designed to describe and relate data on the
Web and inside enterprises\(^1\). Through such technologies human representation of the world and reasoning become machine-interpretable, concluding into powerful knowledge-based systems. Focusing on a domain of interest such systems model the real world artefacts (physical objects, events, relationships, etc) \(^4\) representing knowledge for computational purposes. Reasoning is performed over existing knowledge concluding into new knowledge.

Knowledge in a domain is represented with the use of conceptual models called ontologies\(^2\). An ontology is a formal explicit specification of a shared conceptualization of a domain of interest \(^5\). An ontology constitutes of concepts (Classes), relations (Properties) and instances (Individuals). Concepts represent the ontological categories that are relevant in the domain of interest. For example in BD domain, Therapy and Medicine are main concepts. Instances represent the named and identifiable concrete objects in the domain of interest, i.e. the particular individuals which are classified by concepts such as medicine\(_1\), medicine\(_2\). Relations connect concepts, as well as instances, specifying their interrelations \(^5\), i.e. suggests relation connects the concepts of Therapy and Medicine as well as the defined individuals of these concepts. Standard language for publishing and sharing ontologies is OWL language\(^3\). Web Ontology Language (OWL) is a core W3C standard knowledge representation language for the Semantic Web. It is a highly expressive, flexible and efficient knowledge representation language that can be used to model background knowledge about domains.

Analogously to human reaching, conclusions systems inference conclusions about the stored knowledge through knowledge reasoning. Reasoning is a method of processing background (explicit) knowledge and infers implicit information. SWRL rules perfectly integrate with OWL, making it easy to develop and maintain application systems. Semantic Web Rule Language (SWRL)\(^4\) is the language for specifying rules applying on Semantic Web ontologies. SWRL allows for defining rule expressions involving OWL concepts enabling more powerful deductive reasoning than OWL alone.

OWL represents relations in a binary-form. Binary relations simply connect two instances (e.g., therapy with medicine) without any temporal information as in Fig. 1. The concept of time is introduced in the relations, concluding in ternary relations (e.g therapy suggests medicine between 3 March 2014 and 2 April 2014). Representing ternary relations in the Semantic Web calls for additional methods such as the N-ary approach\(^5\) used in this work.

**Fig. 1 N-ary Representation Model: Ternary relation (above) evolves into binary relations by introducing the new object Event (below)**

The N-ary relations approach suggests representing an n-ary relation as two properties each related with a new object. This approach requires only one additional object for every temporal relation. A temporal property between two individuals (e.g. “Therapy suggests Medicine”) holds as long as that event endures. The n-ary property is represented as a class rather than as a property. Instances of such classes correspond to instances of the relation. Additional properties introduce additional binary links to each argument of the relation. For properties that change in time, their domains and ranges have to be adjusted taking into account the classes of intermediate objects representing the relation. Fig.1 illustrates the static relation between concepts “Therapy” and “Medicine” and its temporal representation based on the N-ary Representation Model.

\(^1\) http://www.cambridgesemantics.com/semantic-university  
\(^2\) http://www.w3.org/standards/semanticweb/ontology  
\(^3\) http://www.w3.org/TR/owl-features  
\(^4\) http://www.w3.org/Submission/SWRL/  
\(^5\) http://www.w3.org/2004/08/12-Yoshio/onNaryRelations.html
Reasoning over temporal information is performed using SOWL approach [6]. SOWL is realized by introducing a set of SWRL rules operating on temporal relations. A temporal relation can be one of the 13 pairwise disjoint Allen’s relations between time points or temporal intervals such as “before”, “after”, “during”, “equals” etc.

Materials and Methods

1.1. Domain Expert and Clinical Guidelines

The AI-CARE system is based on the development of chronic ontology, describing bipolar I disorder (at least one manic or mixed episode), one of the main types of BD according to the Diagnostic and Statistical Manual of Mental Disorders (DSM). Base of our system is the combination of the knowledge received from the domain expert as well as the clinical guidelines and patient data. Through this knowledge we define the domain, the corresponding concepts, and their characteristics. The domain expert can be an expert in BD (a psychiatrist, clinician, biologist etc.) who provide us with information about the domain, support us in decoding the clinical guidelines and designing the treatment’s algorithms.

The clinical practice guidelines, namely the WFSBP6, CANMAT/ISBD7, NICE8, Australian and New Zealand9, and the BAP10 Guidelines, which address the treatment and management of BD compose systematically derived statements that are aimed at supporting clinician decision about bipolar illness [7]. Patient data constitutes the input of our system initializing the Ontology on which the developed rules are applied. BDI patient data refer to all the available demographic-medical-behavioural information of patient’s. Patient’s health records and findings from physical and diagnostic examinations, lab tests, imaging tests (MRS, MRI, (MRI), and different kinds of monitoring tools (mood charting, life charting, antipsychotic and lithium monitoring) can also be used to support the development of AI-CARE system.

1.2. Chronic Ontology for BDI Clinical Scenarios

Based on the information received from the domain experts, clinical guidelines and the patient data, we developed the ontology that represents the domain, the corresponding concepts and the relations between them. In other words, the chronic ontology is generated to govern different clinical scenarios for bipolar illness. Thus, we designed diagnostic scenarios considering the patient history, specific assessments of diagnostic screening instruments (e.g. Mood Disorder Questionnaire, MDQ; World Health Organisation World Mental Health Composite InternationalDiagnostic Interview, WHO WMH-CIDI; structured clinical interview for the DSM-IV, SCID; Bipolar Spectrum Diagnostic Scale, BSDS) and assessments of symptom severity (e.g. Young Mania Rating Scale, YMRS), as well as various findings from physical and diagnostic examinations in order to support initial BDI diagnosis, differential diagnosis, re-evaluation, and prevent misdiagnosis. We also developed treatment scenarios addressing the complex needs of acute treatment (mania, depression), or symptom-free intervals (euthymia) related to the maintenance treatment (relapse prevention, rapid cycling, treatment discontinuation) according to the above evidence-based clinical guidelines, and bipolar treatment algorithms (e.g. TMAP11, PAPHSS12).

As BDI is a rapidly evolving in time mental disorder, the developed ontology evolves in time in order to encode the recorded changes and address the consistent management of these changes [3]. In our implementation, these changes in the domain are reflected in the transition of the static concepts into dynamic concepts. We present this ontology through the class diagram of Fig. 2.

Static entities

- **Patient**: personal information about the patient (first and last name, age, address, sex etc).
- **Episode**: information about the type (manic or depressive) and severity of an episode.
- **Diagnosis**: information about the type of the disorder (Type I or Type II) and if the patient is suffering from rapid cycling or not.
- **PatientHistory**: information about patient’s medical history. Age of onset, heredity, number of manic or depressive episodes, previous medication.

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6 http://www.wfsbp.org/home.html
7 http://www.canmat.org/
8 https://www.nice.org.uk/
9 http://www.healthinfonet.ecu.edu.au/key-resources/promotion-resources?lid=15335
12 http://www.psychopharm.mobi/
- **Standard**: highest and lowest optimal values of each functional test.
- **SideEffect**: possible side effects of a medicine.
- **InitialEvaluation**: initial evaluation for the diagnosis procedure. Initial evaluation is a combination of:
  - **Questionnaire**: Mood questionnaires (MDQ, BSDS, CIDI) for symptoms evaluation, that a patient is called to answer.
  - **History**: History record of a patient that collects a clinician through various questions.
  - **Clinical Evaluation**: the patient is submitted into various functional tests in order to reject other medical causes and ensure psychiatric disorder.
- **Medical Cause**: if the clinical evaluation suggests other medical cause than bipolar disorder.

`Fig. 2 Class Diagram.
Static concepts are distinguished from dynamic concepts

**Dynamic entities (entities which evolve in time):**

- **PHR**: the patient’s medical record.
- **PatientState**: information about the patient’s current state (in euthymia or in an episode).
- **Symptom**: information about the symptom (type, severity).
- **Therapy**: the therapeutic approaches a patient may receive (medication, hospitalization, psychotherapy).
- **Functional Tests**: information about the functional test a patient is submitted. Functional Tests includes various elements that need to be measured. Class TestElement describes the information about each element (name, unit of measure). Subclass Element describes the current value of the element while subclass Standard describes the normal value limits of the element.
- **Medicine**: information about the medicine the patient receives (medicine name, category, dosage etc).

The described classes relate with each other as presented in Fig. 2. Dynamic classes are related with each other during specific intervals. For example class PatientState relates with class Episode during the interval the episode occurs. Main concept in the ontology is class Patient Health Record (PHR). By accessing PHR, we can easily access all the vital information described by the classes which relate with PHR. For example through PHR we can access PatientState and conclude if a patient is in euthymia or not. We start the design with a static ontology describing the main concepts of the Bipolar I Disorder scenario. This initial ontology is developed.
using a common ontology editor such as Protégé Editor\textsuperscript{13}. Then, it is converted to temporal using the CHRONOS\textsuperscript{14} plugin of Protégé.

1.3. Rules and Rules Engine

We inference conclusions about the stored knowledge through the reasoning system implemented in SWRL\textsuperscript{4}. The clinical guidelines are encoded in the form of rules. Rules are the set of asserted facts or axioms expressed in a logical form that together comprise the overall theory that the ontology describes in BDI domain. The rule engine (the piece of software able to infer logical consequences from rules) reasons over the rules, the knowledge and information collected, and provides decisions, alerts and recommendations for the next steps of the treatment. An example of a treatment recommendation rule within mania scenario results in the suggestion of medical treatment. It evaluates the medication the patient is receiving and the type of symptoms the patient presents. In the case that the patient is first diagnosed, receiving no medication and the symptoms suggest existence of a manic episode then the rule directly suggests medical treatment (Lithium, Li; valproate, VAP; atypical antipsychotics, AAP). Necessary information for the rule is included in the classes Personal Health Record (PHR), PatientState, Episode, Therapy, Medicine.

\[ \text{PHR} \cap (\exists \text{PatientState.state} = \text{inEpisode}) \cap (\exists \text{Episode.type} = \text{manic}) \cap \text{Therapy} \cap \lnot (\exists \text{Medicine} \rightarrow \text{Recommendation} \ (\text{Start Therapy with Li/VPA/AAP or combination of two medicines})) \]

Another example of treatment recommendation rule results in the suggestion of dosage optimization of the medicine the patient is receiving. In the case that the patient is receiving medication but he is partially responding to the treatment then the rule suggest dosage optimization. Necessary information for the rule is included in the classes Personal Health Record (PHR), Symptom, Therapy, Medicine.

\[ \text{PHR} \cap (\exists \text{Symptom.severity} = \text{not severe}) \cap \text{Therapy} \cap \exists \text{Medicine} \rightarrow \text{Recommendation} \ (\text{Optimize dosage of medicine}) \]

Overall, our efforts are ongoing and focused on generating rules that cover many issues of the evolution of mental illness diagnosis (presence of symptoms) and treatment (medication compliance, comorbidities, treatment resistance, medication side effects etc.) in order to provide clinicians with a computer-based system able to adjust this knowledge to individual cases according to the clinical judgment and patient preferences after receiving and filtering of relevant available clinical information of patient data.

Notably, we place alerts in crucial decision nodes with supporting annotation from the literature in order to provide the appropriate notifications to the clinicians on real-time such as recommendations of pharmacological treatment including drug dosage, timely alert for medical tests, abnormal (blood) test results, and alerts for medical attention.

1.4. Graphical User Interface

We aim to facilitate easy, friendly access between the user and the system through a user-friendly Graphical User Interface (GUI). Through the User Interface the doctor will be able to insert patient information, retrieve, analyze and process it. The GUI guarantees data availability and valid, on-time alerts and notifications.

Results and Discussion

AI-CARE Framework

Fig. 3 illustrates the AI-CARE clinical decision support system for supporting online the longitudinal monitoring of bipolar patients. AI-CARE framework enhance the utility and accessibility of practice guidelines by clinicians providing support in diagnosis and optimum treatment options, as well as in tracking therapeutic drug safety and tolerability and in preventive care. Considering the domain expert knowledge, the evidence-based clinical guidelines, and the information availability about individual’s health record and patient-centered factors, the AI-CARE system:

- Encodes the available information and links health observations with health knowledge
- Ascribes clinical recommendations/notifications to influence health choices by clinicians for improved health care
- Supports the longitudinal monitoring of the patient’s mental state

\textsuperscript{13} \url{http://protege.stanford.edu/}
\textsuperscript{14} \url{http://www.intelligence.tuc.gr/prototypes.php}
- Informs constantly the psychiatrist about the patient's course of the disease
- Provides emergency scenarios alerting the psychiatrist for non-compliance with drug treatment, mood changes, possible recurrence
- Considers patient's well being and improves the quality of life of patients suffering from the disease, and subsequently enhances the quality of medical health care
- Considers privacy/security issues providing safety in patients’ health records.

![Fig. 3 The AI-CARE clinical decision support system](image)

**Conclusions**

Semantic Web Technologies can support decision-making in mental disorders by encoding its progression in the course of life of bipolar patients, if basic elements of clinical guidelines and patient-centered factors are considered. The chronic ontology model is proposed to illustrate the entire spectrum of BDI and to demonstrate the effectiveness of the CDS system and its potential for clinical use by health care professionals (psychiatrists and primary care physicians).

We present the AI-CARE as a computer-based CDS system with application in BDI. AI-CARE platform enables clinicians to have a useful online tool, which may be requested to monitor the patient’s condition, to provide early-warning signs or notifications for critical mood shifts and retrieve recommendations on best treatment of the patient’s actual state. The validation of AI-CARE system performs progressively to a small sample of clinical cases of bipolar disorder. In the future we aim to extend the current work in order to address other chronic psychiatric or neurological disorders (e.g. epilepsy).

**Acknowledgements**

This work was supported by project "AI-CARE" of the "COOPERATION 2011" framework under the NSRF 2007-2013 Program of the Greek Ministry of Education, Lifelong Learning and Religious Affairs.

**References**